

## **NAPROSYN - naproxen tablet**

bryant ranch prepack

### **DESCRIPTION**

Naproxen is a propionic acid derivative related to the arylacetic acid group of nonsteroidal anti-inflammatory drugs.

The chemical names for naproxen and naproxen sodium are (S)-6-methoxy- $\alpha$ -methyl-2-naphthaleneacetic acid and (S)-6-methoxy- $\alpha$ -methyl-2-naphthaleneacetic

acid, sodium salt, respectively. Naproxen and naproxen sodium have the following structures, respectively:

Naproxen has a molecular weight of 230.26 and a molecular formula of C<sub>14</sub>H<sub>14</sub>O<sub>3</sub>. Naproxen sodium has a molecular weight of 252.23 and a molecular formula of C<sub>14</sub>H<sub>13</sub>NaO<sub>3</sub>.

Naproxen is an odorless, white to off-white crystalline substance. It is lipid-soluble, practically insoluble in water at low pH and freely soluble in water at high pH.

The octanol/water partition coefficient of naproxen at pH 7.4 is 1.6 to 1.8. Naproxen sodium is a white to creamy white, crystalline solid,

freely soluble in water at neutral pH.

NAPROSYN (naproxen tablets) is available as yellow tablets containing 250 mg of naproxen, pink tablets containing 375 mg of naproxen and yellow

tablets containing 500 mg of naproxen for oral administration. The inactive ingredients are croscarmellose sodium, iron oxides, povidone and magnesium stearate.

#### **EC-NAPROSYN**

(naproxen delayed-release tablets) is available as enteric-coated white tablets containing 375 mg of naproxen and 500 mg of naproxen for oral administration. The inactive ingredients are croscarmellose sodium, povidone and magnesium stearate. The enteric coating dispersion

contains methacrylic acid copolymer, talc, triethyl citrate, sodium hydroxide and purified water. The dissolution of this enteric-coated naproxen tablet is pH dependent with rapid dissolution above pH 6. There is no dissolution below pH 4.

ANAPROX (naproxen sodium tablets) is available as blue tablets containing 275 mg of naproxen sodium and ANAPROX DS (naproxen sodium tablets) for oral administration. The inactive ingredients are croscarmellose sodium, povidone and magnesium stearate. The enteric coating dispersion contains methacrylic acid copolymer, talc, triethyl citrate, sodium hydroxide and purified water.

### **CLINICAL PHARMACOLOGY**

Naproxen is a nonsteroidal anti-inflammatory drug

(NSAID) with analgesic and antipyretic properties. The sodium salt of naproxen has been developed as a more rapidly absorbed formulation of naproxen for use as an analgesic. The mechanism of action of the naproxen anion, like that of other NSAIDs, is not completely understood but maybe related to prostaglandin synthetase inhibition.

Naproxen and naproxen sodium are rapidly and completely absorbed from the gastrointestinal tract with an in vivo bioavailability of 95%. The different dosage forms of NAPROSYN are bioequivalent in terms of extent of absorption (AUC) and peak concentration (C<sub>max</sub>); however, the products do differ in their pattern of absorption.

These differences between naproxen products are related to both the chemical form of naproxen used and its formulation. Even with the observed differences in pattern of absorption, the elimination half-life of naproxen is unchanged across products ranging from 12 to 17 hours.

Steady-state levels of naproxen are reached in 4 to 5 days, and the degree of naproxen accumulation is consistent with this half-life.

This suggests that the differences in pattern of release play only a negligible role in the attainment of steady-state plasma levels.

### **INDICATION AND USAGE**

Carefully consider the potential benefits and risks

of NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS or NAPROSYN Suspension and other treatment options before deciding to use NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS or NAPROSYN Suspension. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

Naproxen as

NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS or NAPROSYN Suspension is indicated:

- \* For the relief of the signs and symptoms of rheumatoid arthritis
- \* For the relief of the signs and symptoms of osteoarthritis
- \* For the relief of the signs and symptoms of ankylosing spondylitis
- \* For the relief of the signs and symptoms of juvenile arthritis

Naproxen as NAPROSYN Suspension is recommended for juvenile rheumatoid arthritis in order to obtain the maximum dosage flexibility based on the patient's weight.

Naproxen

as NAPROSYN, ANAPROX, ANAPROX DS and NAPROSYN Suspension is also indicated:

- \* For relief of the signs and symptoms of tendonitis
- \* For relief of the signs and symptoms of bursitis
- \* For relief of the signs and symptoms of acute gout
- \* For the management of pain
- \* For the management of primary dysmenorrhea

EC-NAPROSYN is not recommended for initial treatment of acute pain because the absorption of naproxen is delayed compared to absorption from other naproxen-containing products.

## **CONTRADICTIONS**

NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS and NAPROSYN Suspension are contraindicated in patients with known hypersensitivity to naproxen and naproxen sodium.

NAPROSYN, EC-NAPROSYN,

ANAPROX, ANAPROX DS and NAPROSYN Suspension should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients

NAPROSYN, EC-NAPROSYN,

ANAPROX, ANAPROX DS and NAPROSYN Suspension are contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.

## **ADVERSE REACTIONS**

Adverse reactions reported in controlled clinical trials in 960 patients treated for rheumatoid arthritis or osteoarthritis are listed below. In general, reactions in patients treated chronically were reported 2 to 10 times more frequently than they were in short-term studies in the 962 patients treated for mild to moderate pain or for dysmenorrhea. The most frequent complaints reported related to the gastrointestinal tract.

A clinical study found

gastrointestinal reactions to be more frequent and more severe in rheumatoid arthritis patients taking daily doses of 1500 mg naproxen compared to those taking 750 mg naproxen (see CLINICAL PHARMACOLOGY).

In controlled clinical trials with about

80 pediatric patients and in well-monitored, open-label studies with about 400 pediatric patients with juvenile arthritis treated with naproxen, the incidence of rash and prolonged bleeding times were increased, the incidence of gastrointestinal and central nervous system reactions were about the same, and the incidence of other reactions were lower in pediatric patients than in adults.

In patients taking naproxen in clinical trials, the most frequently reported adverse experiences in approximately 1% to 10% of patients are:

Gastrointestinal

(GI) Experiences, including: heartburn<sup>1</sup>, abdominal pain<sup>1</sup>, nausea<sup>1</sup>, constipation<sup>1</sup>, diarrhea, dyspepsia, stomatitis

Central

Nervous System: headache<sup>1</sup>, dizziness<sup>1</sup>, drowsiness<sup>1</sup>, lightheadedness, vertigo

## OVERDOSAGE

Significant naproxen overdose may be characterized by lethargy, dizziness, drowsiness, epigastric pain, abdominal discomfort, heartburn, indigestion, nausea, transient alterations in liver function, hypoprothrombinemia, renal dysfunction, metabolic acidosis, apnea, disorientation or vomiting. Gastrointestinal bleeding can occur. Hypertension, acute renal failure, respiratory depression, and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose. Because naproxen sodium may be rapidly absorbed, high and early blood levels should be anticipated. A few patients have experienced convulsions, but it is not clear whether or not these were drug-related. It is not known what dose of the drug would be life threatening. The oral LD50 of the drug is 543 mg/kg in rats, 1234 mg/kg in mice, 4110 mg/kg in hamsters, and greater than 1000 mg/kg in dogs.

## DOSAGE AND ADMINISTRATION

Carefully consider the potential benefits and risks of NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS and NAPROSYN Suspension and other treatment options before deciding to use NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS and NAPROSYN Suspension. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals. After observing the response to initial therapy with NAPROSYN, EC-NAPROSYN, ANAPROX, ANAPROX DS or NAPROSYN Suspension, the dose and frequency should be adjusted to suit an individual patient's needs.

Different dose strengths and formulations (ie, tablets, suspension) of the drug are not necessarily bioequivalent. This difference should be taken into consideration when changing formulation. Although NAPROSYN, NAPROSYN Suspension, EC-NAPROSYN, ANAPROX and ANAPROX DS all circulate in the plasma as naproxen, they have pharmacokinetic differences that may affect onset of action. Onset of pain relief can begin within 30 minutes in patients taking naproxen sodium and within 1 hour in patients taking naproxen. Because EC-NAPROSYN dissolves in the small intestine rather than in the stomach, the absorption of the drug is delayed compared to the other naproxen formulations. The recommended strategy for initiating therapy is to choose a formulation and a starting dose likely to be effective for the patient and then adjust the dosage based on observation of benefit and/or adverse events. A lower dose should be considered in patients with renal or hepatic impairment or in elderly patients. Studies indicate that although total plasma concentration of naproxen is unchanged, the unbound plasma fraction of naproxen is increased in the elderly. Caution is advised when high doses are required and some adjustment of dosage may be required in elderly patients. As with other drugs used in the elderly, it is prudent to use the lowest effective dose.

Naproxen-containing products are not recommended for use in patients with moderate to severe renal impairment  
Rheumatoid Arthritis, Osteoarthritis and Ankylosing Spondylitis:

NAPROSYN 250 mg or 375 mg or 500 mg twice daily

275 mg (naproxen 250 mg with 25 mg sodium) twice daily

ANAPROX DS 550 mg (naproxen 500 mg with 50 mg sodium) twice daily

NAPROSYN Suspension 250 mg (10 mL/2 tsp) or 375 mg (15 mL/3 tsp or 500 mg) or (20 mL/4 tsp) twice daily

EC-NAPROSYN 375 mg or 500 mg twice daily.

To maintain the integrity of the enteric coating, the EC-NAPROSYN tablet should not be broken, crushed or chewed during ingestion. NAPROSYN Suspension should be shaken gently before use.

During long-term administration, the dose of naproxen may be adjusted up or down depending on the clinical response of the patient. A lower daily dose may suffice for long-term administration.

The morning and evening doses do not have to be equal in size and the administration of the drug more frequently than twice daily is not necessary.

In patients who tolerate lower

doses well, the dose may be increased to naproxen 1500 mg/day for limited periods of up to 6 months when a higher level of anti-inflammatory/analgesic activity is required. When treating such patients with naproxen 1500 mg/day, the physician should observe sufficient increased clinical benefits to offset the potential increased risk. The morning and evening doses do not have to be equal in size and administration of the drug more frequently than twice daily does not generally make a difference in response .

The use of NAPROSYN Suspension is recommended for juvenile arthritis in children 2 years or older because it allows for more flexible dose titration based on the child's weight. In pediatric patients, doses of 5 mg/kg/day produced plasma levels of naproxen similar to those seen in adults taking 500 mg of naproxen.

The recommended total daily dose of naproxen is approximately 10 mg/kg given in 2 divided doses (ie, 5 mg/kg given twice a day). A measuring cup marked in 1/2 teaspoon and 2.5 milliliter increments is provided with the NAPROSYN Suspension. The following table may be used as a guide for dosing of NAPROSYN Suspension:

Patient's Weight	Dose	Administered as
13 kg (29 lb)	62.5 mg bid	2.5 mL (1/2 tsp) twice daily
25 kg (55 lb)	125 mg bid	5.0 mL (1 tsp) twice daily
38 kg (84 lb)	187.5 mg bid	7.5 mL (1 1/2 tsp) twice daily

The recommended starting dose is 550 mg of naproxen sodium as ANAPROX/ANAPROX DS followed by 550 mg every 12 hours or 275 mg every 6 to 8 hours as required. The initial total daily dose should not exceed 1375 mg of naproxen sodium. Thereafter, the total daily dose should not exceed 1100 mg of naproxen sodium. Because the sodium salt of naproxen is more rapidly absorbed, ANAPROX/ANAPROX DS is recommended for the management of acute painful conditions when prompt onset of pain relief is desired. NAPROSYN may also be used but EC-NAPROSYN is not recommended for initial treatment of acute pain because absorption of naproxen is delayed compared to other naproxen-containing products.

The recommended starting dose is 750 mg of NAPROSYN followed by 250 mg every 8 hours until the attack has subsided. ANAPROX may also be used at a starting dose of 825 mg followed by 275 mg every 8 hours. EC-NAPROSYN is not recommended because of the delay in absorption (see CLINICAL PHARMACOLOGY, INDICATIONS AND USAGE).).

## HOW SUPPLIED

NAPROSYN Tablets: 250 mg: round, yellow, biconvex, engraved with NPR LE 250 on one side and scored on the other. Packaged in light-resistant bottles of 100.

100's (bottle):

NDC 0004-6313-01.

375 mg: pink, biconvex oval, engraved with NPR LE 375 on one side. Packaged in light-resistant bottles of 100.

100's

(bottle): NDC 0004-6314-01.

500 mg: yellow, capsule-shaped, engraved with NPR LE 500 on one side and scored on the other. Packaged in light-resistant bottles of 100.

100's (bottle): NDC 0004-6316-01.

Store at 15° to 30°C (59° to 86°F)

in well-closed containers; dispense in light-resistant containers.

NAPROSYN Suspension: 125 mg/5 mL (contains 39 mg sodium, about 1.5 mEq/teaspoon): Available in 1 pint (473 mL) light-resistant bottles (NDC 0004-0028-28).

Store at 15° to 30°C (59° to 86°F);  
avoid excessive heat, above 40°C (104°F). Dispense in light-resistant  
containers. Shake gently before use.

EC-NAPROSYN Delayed-Release Tablets: 375

mg: white, oval biconvex coated tablets imprinted with NPR-EC 375  
on one side. Packaged in light-resistant bottles of 100.

100's (bottle): NDC 0004-6415-01.

500 mg: white, oblong coated tablets, imprinted with NPR-EC  
500 on one side. Packaged in light-resistant bottles of 100.

100's (bottle): NDC 0004-6416-01.

Store at 15° to 30°C (59° to 86°F)

in well-closed containers; dispense in light-resistant containers.

ANAPROX Tablets: Naproxen

sodium 275 mg: light blue, oval-shaped, engraved with NPS-275 on one  
side. Packaged in bottles of 100.

100's

(bottle): NDC 0004-6202-01.

Store at 15°

to 30°C (59° to 86°F) in well-closed containers.

ANAPROX DS Tablets: Naproxen sodium 550 mg: dark blue, oblong-shaped, engraved with NPS  
550 on one side and scored on both sides. Packaged in bottles of 100.

100's (bottle): NDC 0004-6203-01.

Store at 15° to 30°C (59° to 86°F)

in well-closed containers.

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2007

## **MEDICATION GUIDE APPROVAL**

This Medication Guide has

been approved by the U.S. Food and Drug Administration.

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Label1 : Report

*Aschagat by Dupont Ranch* *Neck, Fullerton, CA 92605*

**Naproxen 250mg Tablet**

Compare To  
Naprosyn 250mg Tablet  
GLENNDAK PHARMACEUTICALS, INC. USA

# 30 EXP 03/11  
NDC 6362932021

LOT 11078

250 MG NAPROXEN

Take with food

Keep all drugs out of reach of children

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